

Claims

1. A human modified thioredoxin composed of any of the following polypeptides:

(a) a polypeptide having an amino acid sequence having a

5 substitution of a cysteine residue at position 35 with another amino acid in an amino acid sequence of SEQ ID NO:2;

(b) a polypeptide having an amino acid sequence having a chemically modified cysteine residue at position 35 in the amino acid sequence of SEQ ID NO:2;

10 (c) a polypeptide having an amino acid sequence having one or more substituted, deleted, inserted or added amino acids in positions except for positions 32 and 35, preferably positions 32 to 35 in the amino acid sequence of SEQ ID NO:2, and having an apoptosis-inducing activity; and

15 (d) a polypeptide encoded by a DNA encoding a human modified thioredoxin having the substitution of the cysteine residue with another amino acid in the amino acid sequence of SEQ ID NO:2 or a DNA capable of hybridizing with a complementary chain thereof under a stringent condition.

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2. The human modified thioredoxin according to claim 1 wherein said another amino acid residue is serine.

3. A gene composed of any of the following DNA and encoding a

human modified thioredoxin having an apoptosis-inducing activity:

(1) a polynucleotide encoding a polypeptide having an amino acid sequence having a substitution of a cysteine residue at position 35 with another amino acid in an amino acid sequence of SEQ ID NO:2

5 and further having one or more substituted, deleted, inserted or added amino acids in positions except for positions 32 and 35, preferably positions 32 to 35 in the amino acid sequence of SEQ ID NO:2, and having an apoptosis-inducing activity, or a complementary chain thereof; and

10 (2) a DNA encoding a human modified thioredoxin having the substitution of the cysteine residue at position 35 with another amino acid in the amino acid sequence of SEQ ID NO:2 or a DNA capable of hybridizing with a complementary chain thereof under a stringent condition and encoding a polypeptide having an apoptosis activity.

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4. A recombinant expression vector expressibly incorporating the gene of claim 3.

5. A transformant transformed with the expression vector of
20 claim 4.

6. A method for producing a polypeptide having an apoptosis-inducing activity, the method comprising culturing the transformants of claim 5.

7. A polypeptide for cell internalization of a biologically active substance comprising an amino acid sequence represented by -Cys-Gly-Pro-A, -Cys-Pro-Tyr-A-, -Cys-Pro-His-A- or

5 -Cys-Pro-Pro-A- (A represents any amino acid other than Cys).

8. Use of a polypeptide comprising an amino acid sequence represented by -Cys-Gly-Pro-A, -Cys-Pro-Tyr-A-, -Cys-Pro-His-A- or -Cys-Pro-Pro-A- (A represents any amino acid other than Cys) for

10 cell internalization of a biologically active substance.

9. A method for producing a biologically active substance complex capable of being internalized into cells, the method comprising binding the biologically active substance to a

15 polypeptide comprising an amino acid sequence represented by

-Cys-Gly-Pro-A, -Cys-Pro-Tyr-A-, -Cys-Pro-His-A- or

-Cys-Pro-Pro-A- (A represents any amino acid other than Cys).

10 A biologically active substance complex capable of being

20 internalized into cells wherein the biologically active substance is bound to a polypeptide comprising an amino acid sequence

represented by -Cys-Gly-Pro-A, -Cys-Pro-Tyr-A-, -Cys-Pro-His-A- or

-Cys-Pro-Pro-A- (A represents any amino acid other than Cys).

11. The complex according to claim 10 wherein the polypeptide comprising an amino acid sequence represented by -Cys-Gly-Pro-A, -Cys-Pro-Tyr-A-, -Cys-Pro-His-A- or -Cys-Pro-Pro-A- (A represents any amino acid other than Cys) is the polypeptide having an amino acid sequence having a substitution of a cysteine residue at position 35 with another amino acid in an amino acid sequence of SEQ ID NO:2.

12. The complex according to claim 10 or 11 wherein the above biologically active substance is a protein or a polypeptide.

13. A method for producing a polypeptide complex capable of being internalized into cells, the method comprising culturing transformants transformed with a recombinant vector having a polynucleotide encoding the complex in which a biologically active polypeptide has been bound to a polypeptide comprising an amino acid sequence represented by -Cys-Gly-Pro-A, -Cys-Pro-Tyr-A-, -Cys-Pro-His-A- or -Cys-Pro-Pro-A- (A represents any amino acid other than Cys).

14. An anti-cancer agent composed of the modified thioredoxin of claim 1 or 2.

15. An anti-cancer enhancer composed of the modified thioredoxin

of claim 1 or 2.

16. An anti-cancer agent composition comprising the modified thioredoxin of claim 1 or 2 and another anti-cancer agent.

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17. A method for treating a cancer, the method comprising administering the modified thioredoxin of claim 1 or 2, if necessary, in combination with another anti-cancer agent to a patient with cancer.

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18. A medicine or a pharmaceutical composition comprising the complex of any of claims 10 to 12 and if necessary a pharmaceutically acceptable carrier, excipient or diluting agent.

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